Widespread Erosions in Intertriginous Areas

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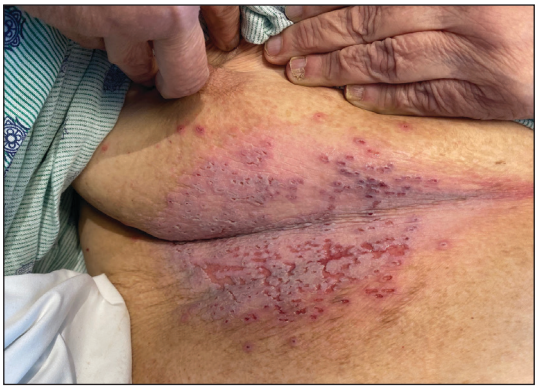

A 72-year-old woman presented to the emergency department with painful, erythematic, pruritic, and purulent lesions in intertriginous regions including the inframammary, infra-abdominal, and inguinal folds with a burning sensation of 1 week's duration. Her medical history was notable for obesity and major depressive disorder. She was empirically treated for cellulitis, but there was no improvement with cefazolin or clindamycin. Dermatology was consulted. Physical examination revealed gray-brown, slightly umbilicated papules in the inframammary region that were malodorous upon lifting the folds. Grouped, punched-out ulcerations with scalloped borders were superimposed onto these papules. Further examination revealed a macerated erythematous plaque in the infra-abdominal and inguinal regions with punched-out ulcers. Hemecrusted papules were observed in seborrheic areas including the anterior neck, hairline, and trunk. Few subtle keratotic pits were localized on the palms. She reported similar flares in the past but never saw a dermatologist and noted that her father and sister had similar papules in a seborrheic distribution. Nail abnormalities included red and white alternating subungual streaks with irregular texture including *V* nicking of the distal nails.

WHAT'S YOUR **DIAGNOSIS?**

a. atopic dermatitis
b. cellulitis
c. Darier disease
d. Grover disease
e. Hailey-Hailey disease

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The authors report no conflict of interest.
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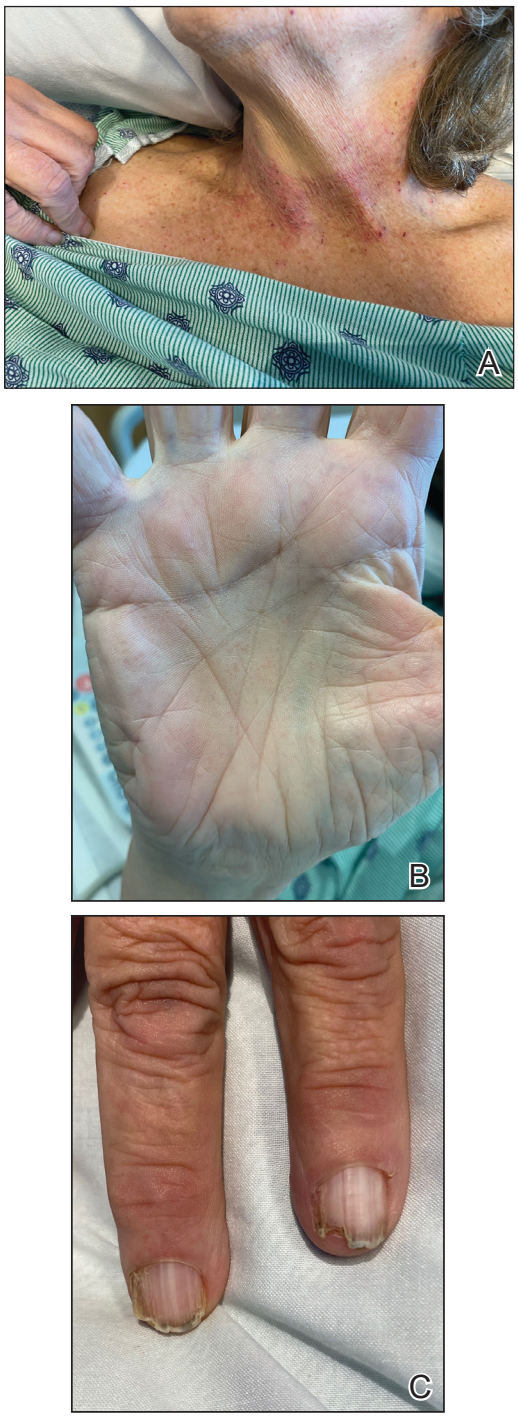
THE **DIAGNOSIS:** Darier Disease

A clinical diagnosis of Darier disease was made from the skin findings of pruritic, malodorous, keratotic papules in a seborrheic distribution and pathognomonic nail dystrophy, along with a family history that demonstrated autosomal-dominant inheritance. The ulcerations were suspected to be caused by a superimposed herpes simplex virus (HSV) infection in the form of eczema herpeticum. The clinical diagnosis was later confirmed via punch biopsy. Pathology results demonstrated focal acantholytic dyskeratosis, which was consistent with Darier disease given the focal nature and lack of acanthosis. The patient's father and sister also were confirmed to have Darier disease by an outside dermatologist.

Darier disease is a rare keratinizing autosomal-dominant genodermatosis that occurs due to a mutation in the *ATP2A2* gene, which encodes a sarco/endoplasmic reticulum calcium ATPase pump that decreases cell adhesion between keratinocytes, leading to epidermal acantholysis and dyskeratosis and ultimately a disrupted skin barrier.[1,2] Darier disease often presents in childhood and adolescence with papules in a seborrheic distribution on the central chest and back (Figure, A); the intertriginous folds also may be involved. Darier disease can manifest with palmoplantar pits (Figure, B), a cobblestonelike texture of the oral mucosa, acrokeratosis verruciformis of Hopf, and nail findings with alternating red and white longitudinal streaks in the nail bed resembling a candy cane along with characteristic *V* nicking deformities of the nails themselves (Figure, C). Chronic flares may occur throughout one's lifetime, with patients experiencing more symptoms in the summer months due to heat, sweat, and UV light exposure, as well as infections that irritate the skin and worsen dyskeratosis. Studies have revealed an association between Darier disease and neuropsychiatric conditions, including major depressive disorder, schizophrenia, and bipolar disorder.[3,4]

The skin barrier is compromised in patients with Darier disease, thereby making secondary infection more likely to occur. Polymerase chain reaction swabs of our patient's purulent ulcerations were positive for HSV type 1, further strengthening a diagnosis of secondary eczema herpeticum, which occurs when patients have widespread HSV superinfecting pre-existing skin conditions such as atopic dermatitis, Darier disease, and Hailey-Hailey disease.[5-7] The lesions are characterized by a monomorphic eruption of umbilicated vesicles on an erythematous base. Lesions can progress to punched-out ulcers and erosions with hemorrhagic crusts that coalesce, forming scalloped borders, similar to our patient's presentation.[8]



Characteristics of Darier disease. A, Gray-brown, heme-crusted papules on the anterior neck. B, A few subtle keratotic pits were noted on the palm. C, Red and white, candy cane–like, subungual streaks on the nail bed with *V* nicking/ridging of the distal nails.

Hailey-Hailey disease, a genodermatosis that alters calcium signaling with an autosomal-dominant inheritance pattern, was unlikely in our patient due to the presence of nail abnormalities and palmar pits that are characteristic of Darier disease. From a purely histopathologic standpoint, Grover disease was considered with skin biopsy demonstrating acantholytic dyskeratosis but was not compatible with the clinical context. Furthermore, trials of antibiotics with group A *Streptococcus* and *Staphylococcus aureus* coverage failed in our patient, and she lacked systemic symptoms that would be supportive of a cellulitis diagnosis. The punched-out lesions suggested that an isolated exacerbation of atopic dermatitis was not sufficient to explain all of the clinical findings.

Eczema herpeticum must be considered in the differential diagnosis for patients with underlying Darier disease and widespread ulcerations. Our patient had more recent punched-out ulcerations in the intertriginous regions, with other areas showing later stages of confluent ulcers with scalloped borders. Delayed diagnosis and treatment of eczema herpeticum combined with severe Darier disease can lead to increased risk for hospitalization and rarely fatality.[8,9]

Our patient was started on intravenous acyclovir until the lesions crusted and then was transitioned to a suppressive dose of oral valacyclovir given the widespread distribution. The Darier disease itself was managed with topical steroids and a zinc oxide barrier, serving as protectants to pathogens through microscopic breaks in the skin. Our patient also had a mild case of candidal intertrigo that was exacerbated by obesity and managed with topical ketoconazole. Gabapentin, hydromorphone, and acetaminophen were used for pain. She was discharged 10 days after admission with substantial improvement of both the HSV lesions and the irritation from her Darier disease. At follow-up visits 20 days later and again 6 months after discharge, she had been feeling well without any HSV flares.

The eczema herpeticum likely arose from our patient's chronic skin barrier impairment attributed to Darier disease, leading to the cutaneous inoculation of HSV. Our patient and her family members had never been evaluated by a dermatologist until late in life during this hospitalization. Medication compliance with a suppressive dose of oral valacyclovir and topical steroids is vital to prevent flares of both eczema herpeticum and Darier disease, respectively. This case highlights the importance of dermatology consultation for complex cutaneous findings, as delayed diagnosis and treatment can lead to increased morbidity and mortality.

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